

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**In re application: **Wallace A. Longton et al.**Serial No.: **09/493,891**Examiner: **Maier, Leigh C**Filed: **January 28, 2000**Group Art Unit: **1623**Attorney Docket: **LEH-35-98**Date: **March 22, 2005****For: LACTONES OF CARBOXYLIC ACID POLYSACCHARIDES AND METHODS  
FOR FORMING CONJUGATES THEREOF**

<b>CERTIFICATE OF MAILING/TRANSMISSION UNDER 37 C.F.R. 1.13(b)(1)</b>			
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Donna J. Mays			

**SUBMISSION WITH REQUEST FOR CONTINUED EXAMINATION**  
**Under 37 CFR 1.114****AMENDMENT AND RESPONSE TO FINAL OFFICE ACTION**

Mail Stop RCE  
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P.O. Box 1450  
Alexandria, VA 22313-1450

Sir or Madam:

This Submission is submitted as part of a Request for Continued Examination (RCE) under 37 CFR 1.114 of the above-referenced patent application, and consists of an Amendment and Response to a Final Office Action mailed October 20, 2005, with a shortened statutory period for responding set to expire January 20, 2005. This RCE Submission was originally filed

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on February 18, 2005, with an accompanying Petition requesting an extension of time in which to reply, which would extend the period for response to February 20, 2005; therefore, upon granting of the Petition, this RCE and Submission were timely filed.

However, the submitted Amendments were considered non-compliant, as explained in an Office Action mailed on March 2, 2005, on the bases that each claim has not been provided with the proper status identifier and that the status identifier for Claim 9 was incorrect. The Applicants were given one month to supply the corrected section which complies with 37 CFR 1.121.

The Applicants are submitting this corrected RCE Submission, in which the proper status identifier of each claim is presented and the status identifier for Claim 9 corrected to "Previously Presented," along with two copies each of the original Request for Continued Examination and the original Petition for extension of time; this RCE Submission is therefore in compliance with 37 CFR 1.121. Moreover, this corrected RCE Submission is filed on March 22, 2005, and is therefore timely filed, and no further fees are believed to be due with this RCE Submission. However, if necessary, please charge any additional fees due, including any fees necessary for extensions of time, or credit any overpayments, to Deposit Account No. 032634.

Applicants respectfully request reconsideration of the application in view of the following amendments and remarks.

**Amendments to the Claims** are reflected in the listing of claims which begins on page 3 of this Submission.

**Remarks/Arguments** begin on page 8 of this Submission.

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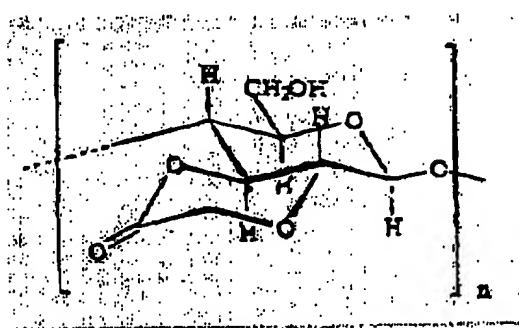
## AMENDMENTS

### To the Claims:

This listing of claims will replace all prior versions, and listings, of the claims in the application:

### Listing of Claims:

1. (Withdrawn) A carboxymethyl cellulose compound according to the formula:



wherein "n" is an integer from 500 to 2000.

2. (Withdrawn) A carboxymethyl cellulose compound according to Claim 1 wherein "n" is an integer from 1000 to 15000.

3. (Currently Amended) A method for the synthesis of a lactone of polysaccharide carboxylic acids which comprises (i) providing the free acid form of the polysaccharide as a finely-powdered, anhydrous carboxylic acid with minimal sodium and potassium carboxylate content; (ii) lactonizing said polysaccharide by thermal dehydration for a period greater than five hours in an anhydrous non-nucleophilic solvent; and (iii) collecting the resulting lactone product, wherein said polysaccharide carboxylic acid is selected from the group consisting of carboxy- and carboxymethyl cellulose, carboxy- and carboxymethyl cyclodextrin, carboxy- and carboxymethyl starch, carboxy- and carboxymethyl chitosan, and pectin.

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4. (Cancelled)

5. (Currently Amended) A method according to Claim 3 which ~~further comprises~~ conducting said lactonization in a refluxing media wherein the solvent is selected from the group consisting of xylene, toluene, diglyme, and acetonitrile.

6. (Currently Amended) A method according to Claim 5 wherein the polysaccharide carboxylic acid is carboxymethyl-cellulose and the solvent is diglyme. Lactonizing consists of:

- (i) suspending the carboxymethyl cellulose in anhydrous diglyme;
- (ii) heating the suspension to about 150°C for about 24 hours;
- (iii) removing the diglyme solvent; and
- (iv) collecting the lactone.

7. (Currently Amended) A method according to Claim 5 wherein the polysaccharide carboxylic acid is pectin acid and the solvent is toluene. Lactonizing consists of:

- (v) (i) suspending the pectin in anhydrous toluene;
- (vi) (ii) heating the suspension for about 24 hours;
- (vii) (iii) removing the toluene solvent; and
- (viii) (iv) collecting the lactone.

8. (Currently Amended) A method according to Claim 5 wherein the polysaccharide carboxylic acid is carboxymethyl-starch and the solvent is diglyme. Lactonizing consists of:

- (i) converting the starch to the free acid;
- (ii) suspending the free acid in anhydrous diglyme;
- (iii) heating the suspension;
- (iv) removing the diglyme solvent; and

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(\*)—collecting the lactone.

9. (Previously Presented) A polysaccharide carboxylic acid lactone product made in accordance with the method of Claim 3.

10. (Withdrawn) A method of forming a polysaccharide carboxylic acid lactone conjugate which comprises (i) ring-opening a polysaccharide carboxylic acid lactone selected from the group consisting of carboxymethyl cellulose, carboxymethyl alpha- and beta- dextran, carboxymethyl starch, chitosan, O,N-Carboxymethyl, O-carboxymethyl, N-carboxymethylchitosan, carboxy-starch, and pectin lactones; and (ii) coupling said lactone with a compound having a biological response within a targeted end-user.

11. (Withdrawn) A method according to Claim 10 wherein ring opening is accomplished with a nucleophilic compound.

12. (Withdrawn) A method for the synthesis of a therapeutic compound comprising the step of conjugating a therapeutic agent to a carboxymethyl polysaccharide utilizing a reactive lactone of said carboxymethyl polysaccharide.

13. (Withdrawn) A method according of Claim 12 wherein the carboxymethyl polysaccharide is carboxymethyl cellulose, and wherein the therapeutic agent is selected from the group consisting of cisplatin, ellipticinium, aminoglutethimide, mitoxantrone, finasteride, vitamin E, alpha-difluoromethylornithine, mitoguazone, and nucleophilic chemotherapeutic agents.

14. (Withdrawn) A method for the synthesis of a conjugated polymer comprising the step of conjugating an agent to a carboxymethyl polysaccharide utilizing a reactive lactone of said carboxymethyl polysaccharide, and wherein said agent is selected from the group consisting of

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an imaging diagnostic capable of binding radioactive metal ions for nuclear imaging or paramagnetic metal ions for magnetic resonance imaging, fragrances, flavorants, cis 3-hexen-1-ol, and property modifiers.

15. (Cancelled)

16. (New) A polysaccharide carboxylic acid lactone product made according to a method for the synthesis of a lactone of polysaccharide carboxylic acids comprising:

- (i) providing the free acid form of the polysaccharide as a finely-powdered, anhydrous carboxylic acid with minimal sodium and potassium carboxylate content;
- (ii) lactonizing said polysaccharide by heating in an anhydrous non-nucleophilic solvent; and
- (iii) collecting the resulting lactone product,

wherein said polysaccharide carboxylic acid is selected from the group consisting of carboxy- and carboxymethyl cellulose, carboxy- and carboxymethyl cyclodextrin, carboxy- and carboxymethyl starch, carboxy- and carboxymethyl chitosan, and pectin, and wherein said polysaccharide carboxylic acid lactone is free of residual chemical activators and promoters.

17. (New) A polysaccharide carboxylic acid lactone product made in accordance with the method of Claim 16, wherein said polysaccharide carboxylic acid is carboxymethyl cellulose.

18. (New) A polysaccharide carboxylic acid lactone product made in accordance with the method of Claim 16, wherein said polysaccharide carboxylic acid is pectin.

19. (New) A polysaccharide carboxylic acid lactone product made in accordance with the method of Claim 16, wherein said polysaccharide carboxylic acid is carboxymethyl starch.

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20. (New) A polysaccharide carboxylic acid lactone product made in accordance with the method of Claim 16, wherein said polysaccharide carboxylic acid is carboxymethyl cyclodextrin.
21. (New) A polysaccharide carboxylic acid lactone product made in accordance with the method of Claim 16, wherein said polysaccharide carboxylic acid is carboxymethyl chitosan.
22. (New) A polysaccharide carboxylic acid lactone product made in accordance with the method of Claim 16, wherein said polysaccharide carboxylic acid is carboxy starch.
23. (New) A polysaccharide carboxylic acid lactone product made in accordance with the method of Claim 3, wherein said polysaccharide carboxylic acid is selected from the group consisting of carboxy- and carboxymethyl cyclodextrin, carboxy- and carboxymethyl starch, carboxy- and carboxymethyl chitosan, and pectin.

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